List B File

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

FEB 21 1997

MEMORANDUM

Subject: Permethrin (List B, Case 2510, Chemical 109701). Magnitude of the Residue in/on Cherries. IR-4. DP Barcode D231288. CBRS 17640. MRID 44135001.

From: Stephen Funk, Chemist
Special Review Section I
Chemistry Branch II - Reregistration Support
Health Effects Division (7509C)

Through: Andrew Rathman, Section Head
Special Review Section I
Chemistry Branch II - Reregistration Support
Health Effects Division (7509C)

To: Paul Lewis
Risk Characterization and Analysis Branch
Health Effects Division (7509C)

In response to the Phase 4 Review, IR-4 has submitted field trial data for cherries. The study was reviewed by Dynamac Corporation under the supervision of CBRS, HED. The review has undergone secondary review by CBRS and has been revised to reflect Agency policies.

The total permethrin residue in/on cherries harvested 3 days after the last of 6 foliar applications of an EC formulation of permethrin at the maximum label rate (0.2 lb. a.i./acre/application) ranged from 0.89 to 3.94 ppm. The current tolerance of 3 ppm was exceeded, and the need for an elevated tolerance will be determined at the time of the *Reregistration Eligibility Decision Document*. No additional field trial data are needed for cherries.

Please advise if additional information is needed.

Attachment: *Permethrin: Registrant's Response to Residue Chemistry Data Requirements (Contract No. 68-D4-0010)*, 01/07/97.

cc with Attachment: S. Funk, RF, Subject File, List B, Patrick Dobak (SRRD).
cc without Attachment: circ.

RDI:A. Rathman:02/19/97:R. Perfetti:02/19/97:
7509C:CBRS:S.Funk:305-5430:CM#2:RM803:SF(0297.2):02/18/97:02/20/97.

Attachment:

PERMETHRIN
Shaughnessy No. 109701; Case 2510
(CBRS No. 17640; DP Barcode D231288)

Registrant's Response to Residue Chemistry Data Requirements

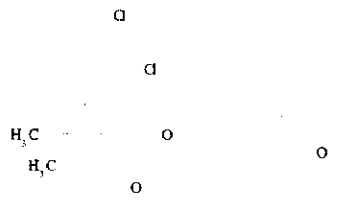
January 7, 1997

Contract No. 68-D4-0010

Submitted to:
U.S. Environmental Protection Agency
Arlington, VA

Submitted by:
Dynamac Corporation
1910 Sedwick Road
Building 100, Suite B
Durham, NC 27713

Permethrin



(Shaughnessy No. 109701. Case No. 2510)

CBRS No. 17640; DP Barcode D231288

REGISTRANT'S RESPONSE TO RESIDUE CHEMISTRY DATA REQUIREMENTS

BACKGROUND

The Permethrin Phase 4 Review (S. Funk and C. Olinger, 5/91) required data depicting residues of permethrin and its metabolites in/on cherries harvested 3 days following the last of multiple applications of permethrin at the maximum labeled rate. In response, the Interregional Research Project No. 4 (IR-4) has submitted field studies on cherries grown in the Eastern U.S. (1996, MRID 44135001). These data are reviewed here to determine their adequacy in fulfilling residue chemistry data requirements. The Conclusions and Recommendations stated in this review pertain only to storage stability of residues and the magnitude of the residue in plants.

The nature of the residue in plants is adequately understood based on adequate soybean, cabbage, and sweet corn metabolism studies. The HED Metabolism Committee (C. Olinger, 2/1/96) has concluded that the residues of concern in plant commodities are the *cis*- and *trans*-isomers of both permethrin and DCVA. Tolerances are to be expressed in terms of the parent, *cis*- and *trans*-permethrin only, but the risk assessment will consider residues of *cis*- and *trans*-DCVA in addition to the parent compound.

Tolerances for residues of permethrin are currently expressed in terms of permethrin and its metabolites, 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropane carboxylic acid (DCVA) and (3-phenoxyphenyl)methanol (3-PBA) in/on livestock and plant raw agricultural commodities (RACs) [40 CFR §180.378 (b), (c), and (d)], with the exception of cottonseed. Tolerances for residues of permethrin in/on cottonseed (0.5 ppm) are expressed in terms of permethrin *per se* [40 CFR §180.378 (a)]. No food/feed additive tolerances have been established for

residues of permethrin. Adequate methods are available for the enforcement of established tolerances, as currently defined.

Once the U.S. tolerance definition is changed to include only permethrin, the Codex and U.S. tolerance expression for permethrin will be compatible. However, the Codex MRL (CXL) for stone fruits is 2 mg/kg, whereas the U.S. tolerance on cherries is 3 ppm. Issues regarding the compatibility of the U.S. tolerances and Codex MRLs will be addressed when the reregistration eligibility decision for permethrin is made.

CONCLUSIONS AND RECOMMENDATIONS

1. The GC/ECD method (G.H. Fujie and O.H. Fuller, J. Agric. Food Chem., 26, 395-398, 1978) is adequate for determining residues of *cis*- and *trans*-permethrin in/on cherries, and the GC/ECD method (GRAM-5/2) is adequate for determining residues of *cis*- and *trans*-DCVA and 3-PBA in/on cherries. The validated limits of quantitation (LOQs) for these methods are 0.01 ppm for each permethrin isomer, 0.05 ppm for each DCVA isomer, and 0.1 ppm for 3-PBA.

2. The submitted storage stability data are adequate and indicate that in stone fruits stored at -20 C, residues of *cis*- and *trans*-permethrin are stable for up to 19.5 months and residues of *cis*- and *trans*-DCVA and 3-PBA are stable for up for ~18 months.

3a. The submitted residue data (MRID 44135001) on cherries (sweet and tart) are adequate and indicate that the combined residues of *cis*- and *trans*-permethrin are likely to exceed the established 3 ppm tolerance in/on cherries harvested 3 days following the last of multiple applications of permethrin at the maximum label rate. Total residues of permethrin were 0.89-3.94 ppm in/on six cherry samples harvested 3-4 days following the last of six applications of permethrin (3.2 lb/gal EC) each at 0.2 lb ai/A for a total of 1.2 lb ai/A/season (1x the maximum label rate).

3b. Previously submitted residue decline data (MRID 41065803) from five tests on sweet and tart cherries treated with multiple foliar applications at 0.2 lb ai/A (1x) indicated that residues of permethrin (*cis* plus *trans* isomers) were 0.48-4.02 ppm at 0 days posttreatment, 0.47-2.19 ppm at 3 or 4 days posttreatment, and 0.31-2.20 ppm at 7 days posttreatment.

3c. DCVA residues were determined on 18 out of 34 cherry samples. Residues of *cis*- and *trans*-DCVA were each <0.05-0.09 ppm in/on sweet and tart cherries bearing residues of permethrin at 0.89-3.94 ppm.

4. The submitted cherry data are adequate and indicate that residues of permethrin are likely to exceed the established 3 ppm tolerance on cherries harvested 3 days

following the last of six applications each at 0.2 lb ai/A (1x). The available data support a tolerance of 4 ppm, and the tolerance will be evaluated at the time of issuance of the *Reregistration Eligibility Decision Document*.

DETAILED CONSIDERATIONS

Residue Analytical Methods

In conjunction with the magnitude of the residue field studies on cherries (1996; MRID 44135001), IR-4 submitted descriptions of GC/ECD methods for analysis of permethrin and its metabolites DCVA and 3-PBA. Sample analyses were performed by the Analytical Testing Laboratory of the Pesticide Research Center, Michigan State University, East Lansing, MI.

Residues of *cis*-and *trans*-permethrin were determined using a GC/ECD method (*Determination of FMC 33297 residues in plant, animal, and soil matrices by gas chromatography*. G.H. Fujie and O.H. Fuller, J. Agric. Food Chem., 26, 395-398, 1978) with minor modifications. In brief, residues are extracted with hexane:isopropanol (2:1; v:v), filtered, partitioned with a 10% NaCl solution, and concentrated. Residues are then purified by gel permeation and Florisil column chromatography, and analyzed by GC/ECD. The LOQ is 0.01 ppm for each isomer.

Residues of *cis*- and *trans*-DCVA and 3-PBA were determined using Zeneca's GC/ECD Method GRAM-5/2 with minor modifications. In this method, residues are extracted with acetonitrile (ACN) followed by ACN:1N HCl (1:1, v/v). The resulting extracts are pooled, filtered, adjusted to pH 9-10, washed with hexane, and concentrated to remove the ACN. Residues are then acidified to pH <0.3, refluxed for 1 hour, and partitioned into hexane. Residues are derivatized using a mixture of pyridine, trichloroethanol, and heptafluorobutyric anhydride (HFBA) in toluene to simultaneously yield the HFB-ester of 3-PBA and trichloroethyl esters of the DCVA isomers. The derivatized residues are then partitioned into hexane, purified by Florisil column chromatography, and analyzed by GC/ECD. The LOQ is 0.1 ppm for 3-PBA and 0.05 ppm for each DCVA isomer.

For method validation, control samples of cherry were fortified separately with permethrin isomers at 0.01-6.9 ppm, DCVA isomers at 0.05 and 0.1 ppm, and 3-PBA at 0.1 ppm. Results of the method validation and concurrent method recovery data are presented in Table 1; method recoveries were 74-122% for permethrin, 73-124% for DCVA, and 70-97% for 3-PBA. Apparent residues of permethrin and its metabolites in/on six control samples of cherry were below the LOQ for each analyte (<0.01 ppm for permethrin isomers, <0.05 ppm for DCVA isomers, and <0.1 for 3-PBA). Sufficient sample calculations, raw data, and representative chromatograms were provided. These data indicate that the above GC/ECD methods are adequate for collecting data on permethrin residues in/on cherries.

Table 1. Method recoveries of permethrin and its metabolites DCVA and 3-PBA from fortified contro samples of cherries using GC/ECD methods.

Analyte	Fortification level (ppm)	Number of samples	% Recovery
Method Validation Data			
cis-permethrin	0.01	3	87, 100, 100
	6.92	3	101, 113, 115
trans-permethrin	0.01	3	110, 111, 115
	5.82	3	94, 101, 110
cis-DCVA	0.05	3	83, 90, 91
trans-DCVA	0.05	3	81, 83, 84
3-PBA	0.10	3	78, 89, 97
Concurrent Recovery Data			
cis-permethrin	0.01	3	95, 111, 118
	0.10	2	93, 114
	6.92	1	114
trans-permethrin	0.01	3	92, 109, 111
	0.10	2	74, 84
	5.82	1	122
cis-DCVA	0.05	3	87, 91, 104
	0.11	1	124
trans-DCVA	0.05	3	73, 90, 96
	0.10	1	96
3-PBA	0.10	4	70, 74, 80, 95

Storage Stability Data

In conjunction with the magnitude of the residue study, IR-4 submitted data on the stability of permethrin, DCVA, and 3-PBA in frozen cherries. Separate control samples of cherries were fortified with permethrin isomers at either 0.1 or ~8 ppm, DCVA isomers at ~0.1 ppm, and 3-PBA at either ~0.1 or ~12 ppm and stored at -20 C. Stored samples were analyzed in triplicate after 258 days (permethrin isomers) and 552-595 days (permethrin and metabolites) along with freshly fortified control samples.

The submitted storage stability data are adequate and indicate that in stone fruits stored at -20 C, residues of *cis*- and *trans*-permethrin are stable for up to 595 days (19.5 months) and residues of *cis*- and *trans*-DCVA and 3-PBA are stable for up for 552-561 days (~18 months).

Table 2. Storage stability of permethrin, DCVA, and 3-PBA in frozen cherries.

Analyte	Fortification level (ppm)	Storage Interval (days)	Uncorrected % Recovery	Corrected % Recovery [a]
cis-permethrin	8.24	258	104, 110, 110	91, 96, 96
	0.10	595	83, 87, 99	99, 104, 106
trans-permethrin	8.55	258	106, 112, 113	87, 92, 93
	0.10	595	65, 66, 70	88, 89, 95
cis-DCVA	0.11	552	99, 104, 116	80, 84, 94
trans-DCVA	0.10	552	80, 95, 95	83, 99, 99
3-PBA	0.12	561	55	82
	11.8	561	62, 51	76, 93

[a] Recoveries of each analyte were corrected using concurrent sample recoveries: *cis*-permethrin (114%, 84%, or 93%), *trans*-permethrin (74% or 122%), *cis*-DCVA (124%), *trans*-DCVA (96%), and 3-PBA (67%).

Samples from the submitted field trials (MRID 44135001) were either transported directly to the analytical laboratory and frozen (-20 C) on the day of collection, or were frozen ($\leq$-20 C) within 1 hour of collection and stored at the field site for up to 24 days prior to shipment by freezer truck to the analytical laboratory. Samples were stored at -20 C at the analytical laboratory. Prior to extraction for analysis, samples were stored frozen for a maximum of 551 days. The available storage stability data adequately support the storage intervals and conditions under which residue samples were held for the current studies.

The available storage stability data on cherry also adequately support field residue studies on cherries (1985, MRID 41065803) previously submitted by FMC, in which cherry samples were stored at -18 C for ~17 months prior to analysis, and field residue studies on peaches (CBRS No. 14290, DP Barcode D207037, C. Olinger, 8/1/95), in which peach samples were stored frozen for up to ~17 months prior to analysis.

Magnitude of the Residue in Plants

Cherries.

A tolerance of 3 ppm has been established for the combined residues of permethrin and its metabolites, DCVA and 3-PBA, in/on cherries [40 CFR §180.378 (b)].

A REFS search dated 7/15/96 listed six permethrin EPs with registered uses on cherries. These EPs included four WP and two EC formulations of permethrin. Permethrin is registered for multiple foliar broadcast applications to cherries at a maximum of 0.2 lb ai/A/application using only ground equipment at a minimum of 25 gal/A. In regions east of

the Rockies, a maximum of six applications is permitted per season, with no more than four applications allowed after petal fall, for a total of 1.2 lb ai/A/season. In regions west of the Rockies, a maximum of four applications is permitted per season, with no more than three applications allowed after petal fall, for a total of 0.8 lb ai/A/season. The labels specify a 3-day PHI and prohibit the grazing of livestock in treated areas or the feeding cover crops from treated areas to livestock.

The Permethrin Phase 4 Review (5/91) required additional data depicting residues of permethrin and its metabolites in/on cherries. In response, IR-4 submitted data (1996; MRID 44135001) from three tests conducted in MI (2) and NJ depicting residues of permethrin and its metabolites, DCVA and 3-PBA, in/on sweet and tart cherries harvested 3 or 4 days following the last of six applications of permethrin (3.2 lb/gal EC) at 0.2 lb ai/A for a total of 1.2 lb ai/A/season. The tests in MI were conducted in 1994 and the test in NJ was conducted in 1995. Applications were made using ground equipment at 100 or 255 gal/A. The four post-bloom applications were applied at 7- to 10-day retreatment intervals.

Two control and two treated samples were collected from each test site 3 or 4 days following the last of six applications. Samples were frozen on the day of sampling and held at $\leq$-20 C for a maximum of 551 days prior to extraction for analysis. The available storage stability data adequately support the storage intervals and conditions under which residue samples were held for the current study.

Residues were determined using the adequate GC/ECD method described in the Residue Analytical Method section of this report. The LOQ is 0.01 ppm for residues of permethrin and 0.05 ppm for residues of DCVA. Apparent residues of permethrin and DCVA were below the LOQs ($<$0.01 or $<$0.05 ppm) in/on the six control samples. Residues of permethrin (*cis* and *trans* isomers) were 0.89-3.94 ppm in/on six cherry samples harvested 3 or 4 days following the last of six applications of permethrin (3.2 lb/gal EC) each at 0.2 lb ai/A for a total of 1.2 lb ai/A/season (Table 3). As in the previous study, the residues were higher on tart cherries than on sweet cherries. Residues of DCVA were $<$0.05-0.09 ppm.

When considered with previously submitted cherry data (MRID 41065803), geographic representation is adequate. A total of eight tests have been conducted on sweet and tart cherries, five in eastern growing regions (MI, NJ, and NY) and three in western (CA, OR, and WA) growing regions.

FMC Corporation previously submitted data (1985; MRID 41065803) from five tests conducted in CA, MI, NY, OR, and WA depicting the decline of permethrin residues in/on sweet and tart cherries harvested from 0 to 7 days following the last of multiple foliar applications of permethrin (3.2 lb/gal EC) each at 0.2 lb ai/A. Tests on sweet and tart cherries were conducted in the West and East, respectively. Except in CA, four applications totaling 0.8 lb ai/A/season (1x) were applied in the West, and six applications totaling 1.2 lb ai/A/season (1x) were applied in the East. Three applications totaling 0.6 lb ai/A/season

(0.75x) were made in CA. All applications were made using ground equipment at retreatment intervals of 9 to 53 days.

Two treated samples were collected from each test site at 0, 3-4, and 7 days following the last application, along with one or two control samples. Samples were frozen on the day of sampling and held at ≤-18 C for a maximum of ~17 months prior to extraction for analysis.

Residues of permethrin were determined using an adequate GC/ECD method having an LOQ of 0.1 ppm. Residues of DCVA and 3-PBA were determined using an adequate GC/mass selective detection method having an LOQ of 0.05 ppm for each metabolite. Metabolite residues were determined in only two tests; the sweet cherry and tart cherry tests having the highest residues of permethrin (NY and WA). Apparent residues of permethrin and DCVA were below the LOQs (<0.1 or <0.05 ppm) in/on all eight control samples.

Residues of permethrin (*cis* and *trans* isomers) were 0.48-4.02 ppm in/on ten samples harvested at the 0-day PTI, 0.47-2.19 ppm in/on ten samples harvested at the 3- or 4-day PTI, and 0.31-2.20 ppm in/on eight samples harvested at the 7-day PTI (Table 4). At the label specified 3-day PHI, residues of permethrin were higher on tart cherries (0.90-2.19 ppm) than sweet cherries (0.47-1.26 ppm). Residues of DCVA were below the LOQ (<0.05 ppm) in all treated samples analyzed.

The submitted cherry data are adequate and indicate that residues of permethrin are likely to exceed the established 3 ppm tolerance on cherries harvested 3 days following the last of six applications each at 0.2 lb ai/A (1x). An increase in the tolerance on cherries may be needed; the available data would support a 4 ppm tolerance.

Table 3. Residues of permethrin and its metabolites, DCVA and 3-PBA, in/on cherries (MRID 44135001) harvested 3 or 4 days following the last of six applications of permethrin at 0.2 lb ai/A, totaling 1.2 lb ai/A/season (1x).

Location (commodity)	Application Data				Residues (ppm)					
	Formulation	Rate (lb ai/A)	Number [a] of Application	PTI [b] (days)	*cis*-Permethrin	*trans*-Permethrin	*cis*-DCVA	*trans*-DCVA	3-PBA	**Total Permethrin** [c]
Fennville, MI (sweet cherry)	3.2 lb/gal EC	0.2	6	3	0.45	0.44	<0.05	<0.05	<0.10	**0.89**
					0.62	0.60	<0.05	<0.05	<0.10	**1.22**
Fennville, MI (tart cherry)	3.2 lb/gal EC	0.2	6	3	1.94	2.00	<0.05	0.06	0.11	**3.94**
					1.51	1.91	<0.05	0.09	0.13	**3.42**
Bridgeton, NJ (tart cherry)	3.2 lb/gal EC	0.2	6	4	0.68	0.51	<0.05	<0.05	0.11	**1.19**
					0.68	0.54	<0.05	<0.05	0.11	**1.22**

[a] Four post-bloom applications were made at 7- to 10-day retreatment intervals.
[b] Days after final application.
[c] Sum of *cis*- and *trans*-permethrin.

Table 4. Residues of permethrin and its metabolites in/on cherries (MRID 41065803, Phase 4 Review, Olinger and Funk, 05/13/91) harvested 0 to 7 days following the last of three to six applications of permethrin (3.2 lb/gal EC) each at 0.2 lb ai/A (1x [a]).

Location (commodity)	Application Data				Residues (ppm)					
	Formulation	Rate (lb ai/A)	Number [b] of Applications	PTI [c] (days)	*cis*-Permethrin	*trans*-Permethrin	*cis*-DCVA	*trans*-DCVA	3-PBA	**Total Permethrin [d]**
Fairfield, CA (sweet cherry)	3.2 lb/gal EC	0.2	3	0	0.30	0.29	NA [e]	NA	NA	**0.59**
					0.34	0.33	NA	NA	NA	**0.67**
				3	0.34	0.33	NA	NA	NA	**0.67**
					0.34	0.32	NA	NA	NA	**0.66**
				7	0.31	0.30	NA	NA	NA	**0.61**
					0.37	0.36	NA	NA	NA	**0.73**
Buena, WA (sweet cherry)	3.2 lb/gal EC	0.2	4	0	0.66	0.72	<0.05	<0.05	<0.1	**1.38**
					0.64	0.70	<0.05	<0.05	<0.1	**1.34**
				3	0.43	0.50	<0.05	<0.05	<0.1	**0.93**
					0.60	0.66	<0.05	<0.05	<0.1	**1.26**
				7	0.49	0.52	<0.05	<0.05	<0.1	**1.01**
					0.59	0.67	<0.05	<0.05	<0.1	**1.26**
Hood River, OR (sweet cherry)	3.2 lb/gal EC	0.2	4	0	0.23	0.26	NA	NA	NA	**0.49**
					0.23	0.25	NA	NA	NA	**0.48**
				3	0.22	0.25	NA	NA	NA	**0.47**
					0.30	0.34	NA	NA	NA	**0.64**
				7	0.19	0.22	NA	NA	NA	**0.41**
					0.14	0.17	NA	NA	NA	**0.31**

(continued; footnotes follow)

Table 4. Continued.

Location (commodity)	Application Data				Residues (ppm)					
	Formulation	Rate (lb ai/A)	Number [b] of Applications	PTI [c] (days)	*cis*-Permethrin	*trans*-Permethrin	*cis*-DCVA	*trans*-DCVA	3-PBA	**Total Permethrin [d]**
Sodus, NY (tart cherry)	3.2 lb/gal EC	6 x 0.2	6	0	1.41	1.36	<0.05	<0.05	0.07	**2.77**
					2.08	1.94	<0.05	<0.05	0.10	**4.02**
				4	1.09	1.10	<0.05	<0.05	0.08	**2.19**
					1.05	1.08	<0.05	<0.05	0.08	**2.13**
				7	1.00	1.02	<0.05	<0.05	0.07	**2.02**
					1.09	1.11	<0.05	<0.05	0.06	**2.20**
Fennville, MI (tart cherry)	3.2 lb/gal EC	0.2	6	0	0.64	0.85	NA	NA	NA	**1.49**
					0.92	1.22	NA	NA	NA	**2.14**
				3	0.39	0.51	NA	NA	NA	**0.90**
					0.80	0.99	NA	NA	NA	**1.79**

[a] The maximum application rate is equal to 4 x 0.2 lb ai/A (0.8 lb ai/A/season) for western regions and 6 x 0.2 lb ai/A (1.2 lb ai/A/season) for eastern regions.

[b] Post-bloom applications were made at 9- to 14-day retreatment intervals, with two exceptions of 25- and 53-day intervals.

[c] Days after final application.

[d] Sum of *cis*- and *trans*-permethrin.

[e] No analysis of metabolite residues was conducted.

MASTER RECORD IDENTIFICATION NUMBER

41065803 Leppert, B. (1985) Determination of Permethrin, Dichlorovinyl Acid and m-Phenoxy-benzyl Alcohol Residues on Cherries Treated with Pounce 3.2 EC Insecticide: Proj. ID RAN-0145. Unpublished study prepared by FMC Corp. 38 p.

44135001 Samoil, K. (1996) Magnitude of Residue: Permethrin on Cherry: Lab Project Number: 05744.94-MIR06: Unpublished study prepared by Interregional Research Project No. 4. 473 p.

AGENCY MEMORANDA CITED IN THIS DOCUMENT

CBRS No.: 14290
DP Barcode: D207037
Subject: Reregistration of Permethrin: Peach Crop Field Trials.
From: C. Olinger
To: P. Lewis
Date: 8/1/95
MRID(s): 43348101

13544

R123758

Chemical: Permethrin

PC Code:
109701
HED File Code: 11100 Other Chemistry Documents
Memo Date: 2/21/1997
File ID: DPD231288
Accession #: 412-06-0193

HED Records Reference Center
7/18/2006